

EDITORIAL COMMENT*

ALLERGIC INACTIVATION OF DIPHTHERIA ANTITOXIN

VIII†

Nine years ago it was shown by Doctor Opie¹ that foreign proteins injected subcutaneously into homologously hypersensitive rabbits are precipitated or otherwise fixed in the local tissues, no appreciable absorption taking place into the blood stream. At the time, this was regarded merely as an interesting grammatical paradox, a local tissue hypersusceptibility functioning as a specific bodily defense. That this phenomenon is of direct clinical significance, however, is currently alleged by Doctor Kahn² of the University of Michigan, who found that, under certain conditions, local allergic fixation of diphtheria antitoxin completely prevents its specific therapeutic action.

Doctor Kahn's allergic studies were made on rabbits previously sensitized to horse proteins, with normal and heterologously sensitized rabbits as the controls. He found that 50 MLD of diphtheria toxin injected intracutaneously into half-grown rabbits invariably causes death in from two to four days. Simultaneous injection of 50 units of diphtheria antitoxin into another cutaneous area almost invariably prevents all demonstrable toxic action. The same antitoxin dose, however, injected into rabbits previously sensitized to horse protein is without this antitoxin effect. All allergic rabbits thus treated died as promptly as the untreated normal or heterologously sensitized controls, autopsies showing typical diphtheria toxin lesions of the adrenal glands.

Doctor Kahn believes that his study "throws light on conditions one frequently meets in children exposed to diphtheria who, after receiving diphtheria antitoxin for passive immunization, contract this disease some weeks later and are then given antitoxin intramuscularly. A severe local inflammatory response usually follows. The results . . . indicate that these children . . . do not derive any curative benefit from the antitoxin, since this reagent undoubtedly remains fixed at the point of injection."

Whether or not routine "desensitization" of his horse-protein-hypersensitive rabbits would render subsequent antitoxin injections therapeutically effective, has not yet been tested by Doctor Kahn.

Stanford University.

W. H. MANWARING,
Palo Alto.

* This department of CALIFORNIA AND WESTERN MEDICINE presents editorial comment by contributing members on items of medical progress, science and practice, and on topics from recent medical books or journals. An invitation is extended to all members of the California and Nevada Medical Associations to submit brief editorial discussions suitable for publication in this department. No presentation should be over five hundred words in length.

† Part I of this series was printed in the February CALIFORNIA AND WESTERN MEDICINE, page 116; Part II in March, page 188; Part III in April, page 275; Part IV in May, page 380; Part V in June, page 447; Part VI in July, page 59; Part VII in August, page 133.

¹ Opie, E. L.: J. Exp. Med., 39:659, 1924.

² Kahn, R. L.: Proc. Soc. Exper. Biol. and Med., 30:611 (Feb.), 1933.

THE LIMITED VALUE OF THE INFORMATION OBTAINED BY A BLOOD CALCIUM DETERMINATION

The note by G. F. Norman¹ in the May number of CALIFORNIA AND WESTERN MEDICINE offers an excellent illustration of the limited value of the total serum calcium determination alone in evaluating diseased states. Since the very limited usefulness of the serum calcium determination is not clearly understood by many physicians, it will be useful to briefly outline the essential facts involved.

In other publications² the authors have pointed out that the calcium of the blood serum exists in several chemical states. Two of these chemical fractions are separable by ultrafiltration into what is commonly termed the diffusible calcium and the nondiffusible calcium. Of these forms, only the calcium determined in the diffusible fraction is a measure of the physiologically available calcium for the control of neuromuscular irritability. The nondiffusible calcium, which is combined with the blood proteins, is quite inert in this respect. The level of the nondiffusible calcium and, therefore, also the level of the total calcium (the total calcium is the calcium ordinarily determined by the routine laboratory procedure) varies with the content of the serum proteins, more particularly the albumin. The level of the blood calcium then may be reduced because of hypoproteinemia. A noted illustration of this occurs in nephrosis, but a hypoproteinemia is by no means limited to this disease and is far more common than has hitherto been suspected. This is well brought out in a recent paper by Moschcovitz.³

Considering, therefore, the complexity of the states of the serum calcium, and the relation of the total calcium and particularly the variation of the nondiffusible calcium fraction with the level of the proteins, it becomes obvious that a simple analysis of the total blood calcium offers practically no information of value in suspect cases of hypocalcemic tetany. If the total blood calcium is slightly lowered, as in Norman's reported cases, it might be so due to a hypoproteinemia rather than to a tetanic phenomenon. If it is normal, it does not rule out the cause of neuromuscular hyperirritability.* To accurately determine the relationship of calcium to tetanic manifestations, it becomes necessary to either determine the level of the diffusible calcium directly or alternatively to rule out hypoproteinemia by a serum protein analysis along with the calcium determination.

From a knowledge of these pertinent facts certain deductions can be drawn regarding the significance of the blood calcium determination.

1. A total serum calcium analysis (normal variations 9.0 to 12.0 milligrams per cent) by itself

¹ Norman, G. F.: A Type of Migraine Associated with Hypocalcemia, Calif. and West. Med., 38:381 (May), 1933.

² The Diffusible Calcium of the Blood Stream. I to V. Arch. of Int. Med., 45:983 (June), 1930; 46:67, 72 (July), 1930; 47:660 (April), 1931; 50:855 (December), 1932.

³ Moschcovitz, E.: Hypoproteinemia, J. Am. Med. Assn., 100:1086 (April 8), 1933.

* The authors have shown that a diffusible calcium of 3.5 milligrams per cent or less is associated with clinical symptoms of active neuromuscular hyperirritability. This phenomenon can be present even when the total calcium is as high as 10.0 milligrams per cent. The lowered level of calcium in such an instance is reflected only in the diffusible calcium, which is very low.